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RUPTURED RIGHT TUBAL PREGNANCY;

ASSOCIATED WITH PERFORATION OF THE VERMIFORM APPENDIX. CONFIRMATORY DIAGNOSIS BY ASPIRATION; OPERATION; DEATH.

By Hunter Robb, M. D., *Resident Gynecologist to the Johns Hopkins Hospital.*

With Remarks by Dr. W. H. Welch.

(Read before the Hospital Medical Society, October 5, 1891.)

Mrs. E. H., colored, aged 23, was admitted to the medical ward of the Johns Hopkins Hospital, March 20, 1891. Prior to admission she was under the care of Dr. Fenby, of Baltimore.

On admission the patient complained of shortness of breath and severe pain in the lower abdomen. She had been perfectly well up to Saturday, one week previous to admission, when she was taken with severe cramps in the abdomen, accompanied by vomiting. Her bowels moved on Saturday, Sunday and Monday, the first three days of her illness, but not afterwards. On Saturday the abdomen began to swell, and she complained of pain all over. Her menses appeared usually at the first of each month, the last one being February the first. She frequently vomited a small amount of greenish brown fluid. Since the preceding Sunday she could only take a small quantity of milk and tea. About one month ago there was a small amount of blood in the stools, the bowels then being loose, but she was not obliged to remain in bed. Owing to the condition of mental hebetude it was difficult to obtain a satisfactory history.

The condition on admission was as follows: Rather anaemic and pale, mucous membranes pale, sclerotic very white; face drawn; temperature between 99° F. and 101° F.; pulse varying from 96 to 130 beats per minute, small, compressible, regular; respirations from 37 to 42. Had some dyspnoea and frequent vomiting of a yellowish green fluid. Lungs were clear in front, in the axillae and behind. Heart dulness at fourth rib and laterally from the left border of the sternum to the mammary line. Apex beat in fifth interspace. Sounds were clear at apex; first sound well marked. Soft systolic murmur heard at pulmonary cartilage. Abdomen symmetrically distended, particularly prominent in the middle, tense, tender on pressure, but tenderness not localized.

Percussion note: tympanitic in upper zone, lower zone dull, right flank tympanitic, left flank slightly resonant. Liver dulness from sixth rib to the costal margin.

Rectal Examination.—Rectum empty; mucous membrane healthy. Patient's temperature during the two days that she was in hospital registered from 99.5° F. on admission, to 101° F. at 12 p. m., and fluctuated between 100° F. and 99° F. to the time of operation.

I saw the patient for the first time on Saturday, March 21, at 1 p. m., one day after admission, in consultation with Dr. Lafleur. By careful inquiry the cessation of the menstrual period for seven weeks was proven. Previously the period had been regular; also with the first cessation of her menstrual period, March 1, she had morning sickness; this continued with more or less severity for two weeks. She also stated that, at intervals, she passed blood-clots, on two occasions resembling shreds of flesh.

On examination of the abdomen it was uniformly distended, with an indistinct sense of fluctuation. On palpation she complained mostly of pain and tenderness in the right flank.

Examination per Vaginam.—Vaginal outlet relaxed, cervical lips œdematous and rather soft; the uterus appeared to be somewhat enlarged, but could not be clearly outlined. There was

fluctuation on both sides of the pelvic cavity, communicated to the vaginal finger by palpation of the abdomen.

Examination of the Breasts.—Mammary glands slightly enlarged. On pressure, some watery, milky fluid exuded. To ascertain definitely the nature of the fluid in the abdomen, at Dr. Lafleur's suggestion, a hypodermic needle was introduced through the abdominal wall, in the median line, midway between the umbilicus and the symphysis pubis, bringing away dark, bloody fluid.

From the clinical history and the general examination I diagnosed ruptured extra-uterine pregnancy. Her general condition at the time of my examination seemed sufficiently good to justify abdominal section. This was clearly her only chance; she was accordingly immediately prepared for operation.

At 3.30 p. m. she was brought to the operating-room, anæsthetized with chloroform, and an abdominal section performed. Upon opening the peritoneal cavity a stream of dark fluid blood, two inches in diameter, spouted seven inches from the incision. As soon as the intra-abdominal pressure was relieved the pulse began to flutter, and the respirations to grow shallow. It was evident that she was rapidly sinking. All the fluid blood was at once washed out with six litres of a sterilized salt solution. As soon as the uterus was palpated the ruptured right tube was recognized. This ruptured portion was about the size of a three-cent piece, with no visible remains of foetal structure attached to it. The tube and ovary were transfixed and incised. The left side was normal. Owing to the feeble condition of the patient further examination of the abdominal cavity was not attempted, and the operation was completed by simply closing the abdominal incision, soon after which life became extinct. Duration of operation fifteen minutes.

By way of criticism I would say, that this is a case which a surgeon would certainly not select for statistics; however, it is one in which it is his moral duty to attempt to relieve. It is the only chance such a patient has, and even if it is one chance in a hundred she certainly should be allowed that chance. I am not able to decide from the specimen, nor from the history, when the rupture occurred. I do not believe it was a recent one. She must have slowly bled to death, as the history which she gave of suddenly being seized with cramps, one week previous to her admission, rather suggests a case in which a leakage takes place, which condition continues until the patient bleeds to death into the abdominal cavity. It is rather an unusual case from the fact that there existed an old suppurative appendicitis, which was completely walled off from the peritoneal cavity. The existence of the appendicular condition was suggested by Dr. Lafleur, in which I concurred, but secondarily to the diagnosis of extra-uterine pregnancy.

From the Pathological Laboratory of the Johns Hopkins Hospital.

Examination of the blood, by Dr. W. S. Thayer, two hours before operation, showed, red corpuscles, 2,281,333; white corpuscles, 15,666; proportion, 1 to 145+. Examination of the dried and stained specimens showed a considerable number of nucleated red corpuscles. The leucocytes showed an excess of polynuclear neutrophiles, as one would expect in a leucocytosis of this degree.

Autopsy.—March 21, at 5 p. m., one hour after death.

Anatomical Diagnosis.—Right tubal pregnancy, isthmial. Rupture of the foetal sac. Extensive hemorrhage into the peritoneal sac. Perforation of the vermiform appendix, causing circumscribed abscess. General acute peritonitis. General anæmia. Marrow in the long bones red and with many nucleated red-blood corpuscles and these also in the circulating blood. Peculiar chronic inflammation, with granular condition of the mucous membrane of the urethra, trigonum vesicæ, left ureter, left renal pelvis, and calyces. Moderate dilatation of left renal pelvis and some of the calyces. Atrophy of the left kidney. Hypertrophy of the muscular wall of the bladder, and of the pelvis of the left kidney. Hemorrhagic decidua in the hypertrophied uterus, corpus luteum of pregnancy in the right ovary. Old perihepatitis and perisplenitis. Cicatrized typhoid ulcer with polypoid thickening of the adjacent mucous membrane. Enlargement of the solitary follicles of the ileum. Old adhesions of the left pleural cavity and circumscribed emphysema of the upper lobe of the left lung. Moderate general pulmonary œdema, bronchitis with foreign particles in the bronchi.

The result of the autopsy as to the organs of the pelvic cavity and surrounding structures is as follows:

Peritoneal Cavity.—The abdominal cavity contains about 30 cc. of dark blood-stained fluid. The visceral and parietal layers of the peritoneum are lined over a large part of their extent with a dark brownish-red membranous layer of coagulated blood, which is rather firmly adherent, but can be stripped off, leaving a comparatively intact peritoneum. The pelvic viscera are covered with coagulated blood. In places there is a thin greyish fibrinous exudation, chiefly on the visceral peritoneum. The coils of the intestines are agglutinated by the blood coagula. There are a number of old fibrous adhesions over the liver and spleen.

Bladder.—Contracted, contains a little fluid, the muscular coats much thickened, the walls measuring 13 mm. in thickness, nearly all of which belongs to the muscle. The mucous membrane is smooth and glistening, but trabeculated in consequence of the hypertrophied ridges of muscles; same over the trigonum vesicae. Here the mucuous membrane presents a dry lustreless thickened appearance, with finely granular surface. The same condition existed in the pelvis of the kidney. This granular appearance is most marked on the side of the trigonum towards the mouth of the left ureter, which is dilated, measuring 2.5 cm. in diameter, whereas the mucous membrane immediately around the mouth of the right ureter looks smooth and glistening. The mucous membrane of the urethra shows in a marked degree the same finely granular appearance of the surface already described; its inner circumference at about the middle is 15 mm. There are the same coarse granulations noticed on the ureteral mucosa as on the other parts similarly affected.

Intestines.—The large intestine contains soft fecal material. The vermiform appendix measures 8 cm. in length, and extends downwards towards the brim of the pelvis. It is enveloped in closely adherent blood coagula. On scraping this away an extensive perforation and sloughing of the wall of the appendix is brought to view. This process is most intense at a distance of 8 cm. from the mouth of the appendix. Over its entire circumference for a distance of 1 cm. in length the wall of the appendix is converted into a dirty grayish-white sloughy mass, and on the median surface at this place there is a sloughy opening, 2 mm. in diameter, communicating with an abscess cavity about 2 cm. in diameter, containing grayish-red purulent material and necrotic shreds. This abscess cavity appears shut in by the surrounding adherent blood laminae, and beneath this some fresh fibrinous

exudation. The vermiform appendix to the distal side of the necrotic patch has thickened walls, measuring 4 mm. in thickness, in which the hypertrophied muscle can be seen. The mucous membrane is covered with a dirty grayish mass of mucus and fibrin, but on scraping this away it is not ulcerated, although it appears thickened and red.

To the peripheral side of the necrosis the lumen of the appendix is narrowed, so as to admit, near the necrotic place, only a fine glass probe, but between this stricture and the mouth of the appendix the lumen is wide, apparently dilated. Just above the ileo-caecal valve the mucous membrane of the ileum over an irregular area, 3 cm. in width and 2 cm. in length, appears slightly depressed and presents a greyish-white fibrous slightly puckered appearance, as if from a cicatrix, and especially in the irregular margins of the apparently cicatricial area there are numerous polypoid-like excrescences of the mucous membrane, 2 to 3 mm. in width, and projecting 2 to 4 mm., sessile with a broad base. (This cicatricial area, with polypoid thickenings of the mucous membranes in the margins, is probably a cicatrized typhoid ulcer). The Peyer's patches in the lower part of the ileum appear prominent, and have an irregular, somewhat reticulated surface, in which the follicles can be seen. The solitary follicles in the lower part of the ileum are swollen, prominent, hard and numerous.

Pelvic Viscera.—The right Fallopian tube and ovary are absent. The tube has been cut away close to the uterus, where the stump is closed by sutures. The left Fallopian tube and ovary appear essentially normal. This tube is free from adhesions, its abdominal mouth patent. It measures 12 cm. in length. The abdominal half of the tube appears a little thickened. The left ovary presents a number of Graafian follicles, several larger than a pea; does not contain a fresh corpus luteum. The uterus is large, its length is 10½ cm. The cervix is 4 cm. in length, the cavity of the body 4.5 cm. The thickness of the wall of the uterus, at the middle of the body is 15 mm., that of the cervix 9 mm. The os externum is widely opened. The entire inner surface of the corpus uteri is covered with a dark red soft mass, which fills the cavity of the body of the uterus.

The site of the mucous membrane of the uterus is occupied by a dark red, almost black tissue about 0.5 to 1 mm. in thickness. In the upper part of the cervical canal is an extension of the same dark red, bloody, tolerably firm material, adherent to the mucous membrane. Elsewhere the cervical canal presents a well-marked arbor vitæ. The mucous membrane of the vagina appears to be normal. All of the pelvic viscera are covered on their peritoneal surface with closely adherent coagulated blood. This blood is firmly adherent and spread out as a distinct membrane in which organization appears to have begun.

Bone-Marrow.—That of the left femur and of ribs is red and contains little fat. Microscopical examination shows red-blood corpuscles, many uninuclear, neutrophilic marrow cells, some with eosinophilic granules, and quite a number of nucleated red-blood corpuscles. The red-blood corpuscles are largely distorted, as in poikilocytosis.

Examination of Specimens Removed at Operation.—They consisted of the ovary and attached Fallopian tube of the right side, and many blood coagula from the peritoneal cavity. The ovary is large, presents one dropsical Graafian follicle the size of a pigeon's egg, and just beneath and by the side of this a large corpus luteum of pregnancy, with thick, yellowish-white festooned wall, and a soft, grayish-red, partly-organized centre. The abdominal extremity of the Fallopian tube is patent, with normal and well-marked fimbriæ. Close to the uterine extremity of the tube where it was cut off, the tube is dilated into a sac about 2 cm. in diameter. This sac is widely ruptured; its inner surface presents a rugous appearance with adherent, dark red masses. The wall of the sac is about 2 mm. in thickness. The blood coagula contain a few small, whitish or grayish particles and some membranous shreds. In these coagula are found typical chorion villi. The blood in these coagula, as well as some withdrawn by Dr. Lafleur before the operation by a hypodermic syringe, shows the most extreme poikilocystosis, pear-shaped, tail-shaped, fusiform, and many other deformities of the red-blood corpuscles.

The microscopical examination of the dark red, bloody, adherent membranes on the surface of the peritoneum shows such a large number of leucocytes that there is undoubtedly a peritonitis, but the inflammatory exudation is obscured by the blood extravasation. Bacteria are found on cover-slips from the bloody material in the peritoneal cavity. The predominating variety are bacilli resembling the bacterium coli commune. The purulent material in the abscess around the perforated vermiform appendix is immensely rich in bacteria of various kinds; not many long forms, mostly short ones, which may be bacterium coli commune. A very few cocci, chiefly in form of diplococci, are present. Cultures in gelatine as roll cultures are made from the peritoneal contents, spleen, liver, and bowels. A cover-slip from the surface of the left renal pelvis does not show any gonococci, but shows a number of short, oval bacteria, which may have gotten there accidentally post-mortem. Cultures made from the blood removed by hypodermic puncture from the abdominal cavity through the abdominal walls midway between the umbilicus and the symphysis pubis, are pure cultures of the bacterium coli commune. This was also obtained in pure cultures on human blood serum from the bloody fluid on opening the abdominal cavity.

It has seemed to me worth while to place this case on record from several points of view. In the first place, it is desirable that a condition as important and interesting as one of extra-uterine fœtation should be recorded. The very extensive hemorrhage which took place in this case, sufficient to distend the peritoneal cavity so that the blood spouted out on opening it at the time of the operation, probably began one week before admission, and it is interesting that it should have been attended with so few characteristic symptoms. An unusual and most serious complication existed in perforation of the vermiform appendix. The condition of the walls of the appendix indicated chronic disease, which may possibly have been present since the attack of typhoid fever, of which positive evidence was found, both in the history and at the post-mortem examination. It is possible that adhesions may have formed between the appendix and the right Fallopian tube, and that the immediate cause of perforation is referable to the condition of tubal pregnancy, but this cannot be positively stated.

It is also interesting to note the sudden collapse of the patient after opening the peritoneal cavity, although her condition before the operation was most grave and gave little promise of a successful issue.

Remarks by Dr. W. H. Welch.

There are many points of interest in this case reported by Dr. Robb. The peculiar form of chronic inflammation, attended

with a granular condition of the mucous membrane of the urethra, extending thence along the left ureter into the left renal pelvis, is probably gonorrhoeal in origin.

Sections of the mucous membrane of the ileum from the areas supposed at the autopsy to correspond to old healed typhoid ulcers, have been carefully studied by Dr. Reed and this diagnosis confirmed. Of special interest is the demonstration of the reproduction of the mucous membrane, containing crypts of Lieberkühn, resting in places directly upon the main muscular coat, where the submucous coat had been destroyed by the ulceration. This specimen shows conclusively that the glands of Lieberkühn are reproduced after typhoid ulceration.

The finding of the bacillus coli communis in large number in the bloody fluid withdrawn by hypodermic syringe during life, suggests the value of a bacteriological examination of the fluids withdrawn for purposes of diagnosis from the peritoneal cavity. The existence of intestinal perforation was suspected in this case, not on the grounds of any symptoms pointing during life to this accident, but simply on the ground of the bacteriological examination. This suspicion was confirmed at the autopsy, which revealed perforative appendicitis. The symptoms referable to this condition were obscured by those resulting from the ruptured sac of tubal pregnancy.

The sudden death in this case during or immediately after the operation, may be explained in the following manner: The abdominal contents, including, of course, the abdominal vessels, were evidently subjected to great pressure from the large amount of blood extravasated into the peritoneal cavity. This is proven by the statement of Dr. Robb, that as soon as the peritoneal cavity was incised a stream of blood two inches in diameter spouted up to a height of seven inches. Now, we know that the abdominal vessels are capable of holding almost the entire amount of blood in the body, so that if the portal vein in a dog be ligated the dog soon dies from the withdrawal from the circulation of the large quantity of blood accumulated in the abdominal vessels. The animal dies, as it were, from hemorrhage into its own blood-vessels. In the present case the sudden lifting off of the pressure on the abdominal vessels by the removal of the blood from the peritoneal cavity permitted the vessels to expand and receive a much larger volume of blood. In consequence of the great reduction in the volume of circulating blood which had already resulted from the intra-peritoneal hemorrhage, this sudden accumulation of blood in the dilated abdominal vessels brought about a condition incompatible with the continuance of the circulation. We know that death from hemorrhage is the result of a diminution in the volume of the blood and not simply of the withdrawal of a nutritive fluid, for just as much good is accomplished by injections of salt solution as by transfusion of blood. What is necessary in such cases is an increase in the volume of fluid in the blood-vessels, and in the present case it was the sudden diminution of this volume in the rest of the circulatory apparatus in consequence of its accumulation in the abdominal vessels, which brought about the final collapse of the already greatly enfeebled circulation. Of course there is only a remote analogy between the conditions in the present case where a sudden extravasation of a large amount of blood had occurred into the peritoneal cavity and soon after this was withdrawn, and the conditions in an ordinary case of chronic ascites where the fluid has accumulated slowly, the vessels have had time to adjust themselves to the altered mechanical conditions and the general volume of circulating blood has not been greatly reduced by previous hemorrhage. We should not therefore expect such an accident to follow the withdrawal of the fluid in an ordinary case of ascites as occurred in the present instance.

NOTES ON NEW BOOKS.

Historical Sketch of the University of Maryland School of Medicine (1807–1890), with an introductory chapter, notices of the Schools of Law, Arts, Sciences and Theology, and the Department of Dentistry, and a general Catalogue of Medical Alumni. By EUGENE FAUNTLEROY CORDELL, M. D. (Class of 1868). (*Baltimore*, 1891.)

The pains-taking industry of Prof. Cordell has rescued from oblivion a most interesting story of the foundation and subsequent history of the University of Maryland School of Medicine. Founded in 1807 by Brown, Davidge, Cocke, Shaw, Bond and others, it was the fifth medical school in the United States in age, the others being at Dartmouth College, Harvard University, the University of Pennsylvania and the College of Physicians and Surgeons, New York. It had the usual vicissitudes of medical schools, being at first without buildings, money, facilities for teaching or library. Later came a long-continued controversy between the Regents and Trustees which divided the faculty and students, and was only settled by an appeal to the courts. Subsequently the Civil War interfered much with its prosperity and development. Notwithstanding all of these disadvantages the University of Maryland has done a most useful work, and has left an abiding impress upon the medical education of the country. To use the words of the author "they (the founders) purchased with their private means a library; they procured costly apparatus from Europe; later they effected a loan and erected another building for lecturing purposes and for the accommodation of the splendid anatomical and pathological collection of over 1,000 specimens which they had bought; early recognizing the need of facilities for clinical instruction, they leased ground in the immediate vicinity of the college, and erected thereon a costly hospital (being among the first, at least, to do this); they encouraged classical learning by founding a gold medal for Latin theses and in other ways. Their successors introduced hygiene and medical jurisprudence into their curriculum (1833); they endeavored to increase the opportunities for instruction by voluntarily lengthening their course to six months (1840); they early taught auscultation and percussion (1841); they instituted lectures on pharmacy (1844); they gave a complete course in operative surgery (1845) and pathology (1847); they encouraged preparatory medical schools; they were either first or second to enforce dissection (1833, 1848); they established compulsory courses in experimental physiology and microscopy (1854); they were among the first to introduce the study of specialties (1866), and first to make an independent chair of diseases of women and children; they established a successful dental school (1882), a lying-in-hospital (1887), and a training school for nurses (1890)." The author has done excellent service to his *alma mater* and to the cause of medical education by his conscientiously-written work. It should be purchased by every alumnus of the school. H.

SPECIMEN OF TRAUMATIC CEREBRAL ABSCESS, WITH BACTERIOLOGICAL EXAMINATION.

By William H. Welch, M. D.

(Meeting of The Johns Hopkins Hospital Medical Society, November 3, 1890).

Dr. Welch showed to the society a brain containing an abscess of the left frontal lobe with the following history:

E. M., negro, aged 26. Ten days before admission patient had been struck on the left side of the forehead, about 1½ inches above the upper border of the orbit, with a grubbing hoe. No particular symptoms developed until the day before admission, when he had what was called a fit. At the time he was working on board of a boat and fell overboard with loss of consciousness. Upon admission there existed a little below and to the outer side of the left frontal eminence a suppurating wound, beneath which was recognized a depressed fracture of the skull. The depressed fragments were elevated and removed. Beneath them the dura mater appeared intact. The patient's general condition after the operation seemed good for several days. He then became inclined to sleep much and seemed dull. His mind and memory were somewhat impaired, but he would answer questions rationally and sometimes he was much brighter mentally than at others. No distinct paralysis could be recognized. He presented no urgent symptoms until a few hours before his death, when he complained of headache and vomited. He passed into a condition of stupor and died somewhat suddenly. Death occurred 64 days after the injury, 50 days after the operation.

At the post-mortem examination, which was made soon after death, with the exception of general pulmonary œdema and moderate swelling of the spleen, the only important lesions were of the skull and brain.

On the left side of the forehead, a short distance below the border of the hair, is a semicircular white scar, 9 cm. in length, healed throughout except over an ulcerated, granulating surface 1.5 cm. in diameter, situated 5 cm. from the median line near the border of the hair. This ulcerated surface corresponds to a round defect in the frontal bone filled with firm gray cicatricial tissue. Upon removing the calvaria the dura mater is found firmly adherent around the margins of this trephined opening and to the cicatricial tissue filling it. The dura is also adherent to the pia-arachnoid membrane of the left frontal lobe over an area 3 cm. in diameter, which corresponds to the hole in the bone. Elsewhere the dura and the pia-arachnoid membranes are free from any inflammatory reaction, there being no acute meningitis. The convexity and the median surface of the left frontal lobe in its anterior part appears swollen, the convolutions somewhat flattened, the pia-arachnoid over this part paler than elsewhere, and upon palpation this part of the brain is softer than the rest and affords a distinct sense of fluctuation. These changes do not extend so far back as the central convolutions. Upon incision the left frontal lobe is found to be the seat of an abscess from which about 50 cc. of creamy, opaque, green pus escapes. The abscess is oval in shape and measures 5.5 cm. in its longest diameter. It occupies the centrum ovale of the anterior part of the frontal lobe, its posterior margin lying 5 cm. in front of the fissure of Rolando. The gray matter is not involved in the abscess except at one point where the abscess extends to the surface of the brain, and here its wall is formed by the thickened pia-arachnoid membrane. This corresponds to an area 1 cm. in diameter where the dura mater, as mentioned above, is adherent to the pia-arachnoid membrane on one side, and to the margins of the hole in the skull and the overlying cicatricial tissue on the other. The spot where the gray matter is thus destroyed by the abscess is in the middle frontal convolution on the convexity 3 cm. behind the anterior pole of the brain, and 2.5 cm. from the median border. The wall of the abscess is formed by a bluish, slate-colored, membranous capsule, averaging 2 mm. in diameter, covered on its inner surface with opaque, greenish-white, adherent material, and surrounded externally by very soft, apparently disintegrated, moist, white brain substance for a distance of 1 cm., the softening gradually merging into normal cerebral substance. The capsule of the abscess is of firm consistence, and readily separates from the surrounding softened brain substance. The pus within the abscess has a deep green color and a very decided, offensive odor of sulphuretted hydrogen. The basal ganglia and internal capsule are normal.

On the surface of the right middle temporal convolution, near the angular gyrus, is a superficial defect about 1 cm. in extent, of a brownish color, covered by pigmented brownish pia-arachnoid. This defect is free from any acute inflammatory reaction and is doubtless the result of contre-coup at the time of the injury. On the inner surface of the dura mater covering the base of the frontal lobe are several thin yellow patches 0.5–1 cm. in diameter, evidently the result of slight hemorrhage. The lateral ventricles contain a slightly increased amount of serum, which is a little turbid. The vessels are normal and there are no other lesions in the brain than those described.

Fresh cover-slip preparations from the pus in the cerebral abscess show a moderate number of cocci. These cocci occur in pairs and in small clumps. They present the appearance of the ordinary staphylococcus pyogenes. None were found inside of cells. The cover-slip preparations were made immediately upon the removal of the brain and without any chance of contamination. Cultures were made from the pus, both by smearing a considerable quantity of the pus over the surface of slanting agar, and by making a set of roll agar cultures. These tubes were kept at body temperature in the thermostat and remained absolutely sterile.

There are several points of interest in connection with this case of cerebral abscess. The direct connection of the injury with the development of the abscess is clear, a straight path being made thereby for the invasion of micro-organisms from without, a path clearly evident at the post-mortem examination. The absence of marked symptoms and their obscure character is explicable by the seat of the abscess in the white matter of the anterior part of the frontal lobe. Had the nature of the affection been recognized a more favorable case for surgical interference could hardly be imagined, in view of the absence of acute meningitis, the strictly localized character of the lesion and the cicatricial adhesions between the wall of the abscess and the overlying tissues at the spot corresponding to the defect in the bone.

The finding of micrococci, presumably the ordinary pyogenic staphylococci, by microscopical examination of the pus and the failure to obtain them in cultivation are points of especial interest. It can hardly be doubted that the micrococci which were found were concerned in the causation of the abscess. Whether they

were the only organisms concerned is uncertain. No other species was found by microscopical examination, but the distinct odor of sulphuretted hydrogen possessed by the pus may point to the existence of some other organism. Still it is possible that the ordinary pyogenic staphylococci are capable of producing that decomposition of the chemical substances composing the brain which yields sulphuretted hydrogen, although in abscesses caused by them in other parts of the body no odor of sulphuretted hydrogen is present. In the long interval which had elapsed after the injury (64 days) the micrococci had evidently died, as is shown by the results of the cultures from the pus. It is not uncommon in very old suppurative processes to obtain negative results with cultures from the pus, and the present case shows conclusively that in such instances the negative result should not be interpreted as evidence that the suppuration was not due to bacteria, for the bacteria which caused the disease may have perished.

DUPLICATURE OF ARCH OF AORTA WITH ANEURISM.

By William H. Welch, M. D.

(Meeting of The Johns Hopkins Hospital Medical Society, February 2, 1891.)

Dr. Welch presented a specimen of duplicature of the aortic arch with aneurism. The specimen came from a negro 43 years old, who for six months before death had suffered from paroxysmal cough, hoarseness increasing to aphonia, dyspnœa increasing to orthopnœa, pain in the chest and loss of flesh. Nineteen years ago he had acute articular rheumatism, and some years before that pneumonia. On admission extreme dyspnœa, inspiration short and noisy, expiration much prolonged and rough. Pulse regular, 132; resp. 36; temp. 97.6° F. Moderate engorgement of superficial veins of neck. Sternal notch obliterated. Heart sounds normal, apex beat neither visible nor palpable. Dulness at third rib and diminished resonance over sternum at this level. Coarse and fine râles over posterior part of both lungs. Respiratory sounds rough. Urine moderately albuminous, with hyaline and granular casts. Patient died suddenly three days after admission to the hospital.

At the autopsy the lungs were found to be moderately emphysematous with slight dilatation of the bronchi. There were numerous areas of fresh broncho-pneumonia in the posterior lobes of both lungs and general pulmonary œdema. The kidneys were small and granular and microscopically showed increase of connective tissue, fibrous glomeruli and atrophied tubes. In the cervical and portal lymphatic glands were encapsulated old caseous nodules. The liver, spleen and alimentary tract presented no noteworthy lesions.

The heart was normal, no changes being present in the valves nor in the size of the heart cavities or the thickness of their walls. On the posterior wall of the ascending aorta, 3 cm. above the valves, is a distinct depression 5 mm. in diameter and 2 mm. in depth, over which the apparently normal intima is continuous. At the point where the innominate artery should be given off the aorta divides into two branches, a larger anterior and a smaller posterior branch which joins the anterior branch 2 cm. below the origin of the left subclavian artery. The posterior branch passes behind the trachea, between it and the œsophagus, so that the trachea passes through the ring formed by the two divisions of the transverse arch of the aorta. From the anterior division are given off in their usual position the left common carotid and the left subclavian arteries. The beginning of the posterior trunk is the seat of a saccular aneurism about the size of a hen's egg, with a somewhat triangular mouth measuring 2 by 1.5 cm. in diameter. The walls of the opening are smooth and the inner surface of the aneurism only a little irregular and rough. The sac contains fluid and red freshly coagulated blood. There are only a few scattered patches of endarteritis in the wall of the aneurism and elsewhere in the course of the aorta, some of these being atheromatous. From the posterior division of the arch are given off the right carotid and subclavian arteries, the former arising from the sac of the aneurism and the latter a short distance beyond this (*i. e.* further from the heart). Beyond the aneurism the posterior division measures 3½ cm. in length and 1 cm. in diameter.

The chief interest in the specimen is the duplicature of the transverse part of the arch of the aorta. This congenital anomaly, as well as others affecting the aortic arch, can be understood only by a consideration of the embryological development of the aorta and its branches, and from this point of view and from that of comparative anatomy these anomalies are of great interest. Duplicature of the transverse arch of the aorta is to be explained by the persistence after birth of conditions belonging to early fœtal life, which should have disappeared in the normal course of development. The fourth right aortic arch (calling the arch nearest the heart the fifth) persists throughout its course and constitutes the posterior division of the arch in our specimen. In normal development the beginning of the right fourth aortic arch becomes the innominate artery from which ascends the right common carotid, corresponding to the prolongation of the right ascending root of the aorta or the beginning of the third right aortic arch. The transverse part of the right fourth aortic arch (the right fourth bronchial artery) becomes the right subclavian, from which the vertebral is given off, and the descending part of the right fourth arch, which in early development unites with the corresponding part of the left fourth arch to make the aorta descendens, is obliterated. It is in the persistence of this descending part of the fourth right aortic arch that the abnormality essentially consists by which the so-called duplicature of the arch of the aorta is produced, and it is interesting to note that in the amphibia this condition is normal, a right as well as a left aortic arch existing.

The first record of an abnormality in the human being similar to that in our specimen appears to be by Hommel in 1737, but in Hommel's case both the œsophagus and the trachea passed through the ring formed by the anterior and the posterior divisions, whereas in our case only the trachea enters the ring. Since Hommel a number of cases of duplicature of the aortic arch presenting considerable diversity in the exact arrangement and the origin of branches in different cases have been recorded. I have not found any case recorded in which the posterior division was the seat of an aneurism as in the present case.

FURTHER STUDIES UPON THE RELATION OF THE PSEUDO-DIPHTHERITIC BACILLUS TO THE DIPHTHERITIC BACILLUS.

By A. C. Abbott, M. D., *Assistant in Bacteriology and Hygiene, Johns Hopkins Hospital.*

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

In a communication recently made by Professor Welch and myself, the results of our bacteriological examination of a series of cases of diphtheria and the reasons for regarding the Klebs-Löffler bacillus as a specific cause of genuine, primary diphtheria, were presented.[1] In this paper we called attention to the unsatisfactory status of the question regarding the so-called pseudo-diphtheritic bacillus. The present communication is intended to shed some light upon this unsettled question.

While there is a general agreement of opinion as to the morphological, cultural, and pathogenic properties of the genuine virulent bacillus diphtheriæ, there is no little confusion as to the nature of the so-called pseudo-diphtheritic bacillus and in general as to the nature of bacilli found in the throat, which, although resembling in many respects the diphtheritic bacillus, still differ from it in some important particulars.

Löffler[2] was the first to use the term pseudo-diphtheritic bacillus, and to call attention to the properties which he considered to differentiate it from the genuine diphtheritic bacillus. By means of agar-plate cultures made from a growth on blood-serum obtained from a case of diphtheria, he isolated two sorts of bacilli, the one corresponding in all respects to the genuine diphtheritic bacillus, the other differing from this organism in the following respects: it was devoid of pathogenic properties for guinea-pigs, its colonies were less distinctly notched at the margins and were whiter than those of the virulent diphtheritic bacillus, it was somewhat smaller than the virulent bacillus, and its ends less frequently swollen. He calls attention to the possibility that there may be several species of bacilli belonging to the same group as the virulent diphtheritic bacillus, as there are several species belonging to the group of the cholera bacillus, and that careful observation of the morphological and biological peculiarities will enable us to distinguish the genuine diphtheritic bacillus from the pseudo-diphtheritic just as we can distinguish the cholera bacillus from other similar species of bacteria.

In 1887 and 1888 von Hoffmann,[3] from the examination of over 60 cases of various kinds, including genuine diphtheria, diphtheritis faucium accompanying scarlatina and measles, simple pharyngeal catarrh, and normal mucous membranes, came to the conclusion that a bacillus resembling the Klebs-Löffler bacillus closely in its morphological and cultural properties but differing from it in certain respects, is a very common, probably regular, inhabitant of the pharynx. This bacillus von Hoffmann identified with the one already described by Löffler as the pseudo-diphtheritic bacillus, and to the differential characters already given by Löffler he added another, viz: that the virulent diphtheritic bacillus grows feebly upon plain nutrient agar, whereas the pseudo-diphtheritic bacillus grows luxuriantly upon this medium, and that, too, at the ordinary temperatures of the room. Von Hoffmann, furthermore, found in diphtheria and other conditions a bacillus indistinguishable from the genuine diphtheritic bacillus in its morphology and behavior on culture media, but devoid of pathogenic properties. In one case of measles and in one case without any affection of the larynx or pharynx, he found a bacillus indistinguishable from the virulent diphtheritic bacillus.

In 1888 Babes[4] published an article, *Ueber isolirt färbbare Antheile von Bacterien*, in which he described various species of bacteria which resemble more or less closely, especially as regards the presence of stained granules in them, the Klebs-Löffler bacilli. Upon the basis especially of this peculiarity and of the property of presenting swollen ends and segments, he distinguished a family group of bacteria, to which belong the Löffler bacillus, the Xerosis bacillus, a bacillus found by him in three cases of trachoma, and also bacilli found by him in the margin of a perforating syphilitic ulcer of the palate and in the spleen and lungs of the same case, and in a case of genuine lobar pneumonia. In a phlegmonous inflammation of the neck, resulting from genuine diphtheria, Babes found a bacillus resembling the Löffler bacillus, but larger and presenting large terminal oval spores. It is evident that in this family group Babes includes bacilli which are readily distinguishable from the Löffler bacillus, as well as some which closely resemble the latter organism.

Orthmann[5] (1889), in a case of apparently diphtheritic affection of the mucous membrane of the cheek, and in a case of purulent meningitis of the convexity, in the exudate and in the nose, isolated a bacillus which he found to be identical with the pseudo-diphtheritic bacillus of Löffler and von Hoffmann, and he confirmed the statements of these observers as to the differential characters of this bacillus.

Kolisko and Paltauf[6] (1889) were able to find the pseudo-diphtheritic bacillus of von Hoffmann only very rarely. They confirmed the statement that this bacillus grows very well upon gelatine and especially upon agar-agar, whereas the genuine diphtheritic bacillus grows feebly on these media, which therefore furnish a useful diagnostic means for distinguishing the two species.

Zarniko[7] (1889) obtained results contradictory in many important details to those of von Hoffmann. He found that the diphtheritic bacillus grows well upon gelatine (as had been previously noted by Orthmann) and upon agar-agar (as had been observed by Flügge). In 29 cases in which the healthy or the catarrhal mucous membrane of the pharynx was examined, he failed to find in a single instance the genuine diphtheritic bacillus, and in only one instance did he find a bacillus which he identified with the pseudo-diphtheritic bacillus. He describes the following characteristics of the pseudo-diphtheritic bacillus: The growth upon Löffler's blood-serum is indistinguishable from that of the diphtheritic bacillus and its temperature limits are the same. On gelatine and upon agar-agar it grows more luxuriantly on the surface, so that glistening white deposits appear in distinction to the delicate grayish-white deposits of the diphtheritic bacillus. A fundamental difference is found in the growth of the two organisms in bouillon. The pseudo-diphtheritic bacillus renders the bouillon cloudy from the third day, and the sediment is more compact and white than in the case of the genuine bacillus. The bouillon retains its alkaline reaction, whereas the diphtheritic bacilius in a short time produces an acid reaction. The rods are somewhat shorter and plumper, and involution and degeneration forms are less common than in the case of the diphtheritic bacillus. It is devoid of pathogenic properties for guinea-pigs, rabbits and white mice. Zarniko found the diphtheritic bacillus to be in all cases pathogenic for guinea-pigs.

Escherich[8] (1890) found the pseudo-diphtheritic bacillus only twice and infers that the circumstances of von Hoffmann's investigations must have been of a very unusual character. Escherich bases the distinction between the pseudo-diphtheritic bacillus and the diphtheritic bacillus upon characters noted by previous observers, viz.: for the former, the pure white color of the colonies, the richer growth upon agar, the cloudiness and permanently alkaline reaction of the bouillon, and the microscopic examination. These differential characters he considers sufficient for the diagnosis. He says that in no case did he find bacilli morphologically and in cultures identical with the Löffler bacillus, but devoid of pathogenic properties when tested upon animals.

Klein[9] (1890) found in the examination of 22 cases of diphtheria two

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1 Welch and Abbott, *The Johns Hopkins Hospital Bulletin*, 1891, No. 11.

2 Löffler, *Centralblatt f. Bacteriologie u. Parasitenkunde*, 1887, Band II, p. 105.

3 Von Hoffmann, *Tagebl. d. 60 Versamml. Deutscher Naturf. u. Aerzte in Wiesbaden*, 1887, p. 119, and *Wiener Med. Wochenschrift*, 1888, No. 3 u. 4. (Quoted from *Baumgarten's Jahresbericht*, 1887, p. 245.

4 Babes, *Zeitschrift f. Hygiene*, Bd. V., p. 173.

5 Orthmann, *Berliner Klin. Wochenschrift*, 1889, No. 10, p. 218.

6 Kolisko and Paltauf, *Wiener Klin. Wochenschrift*, 1889, No 8.

7 Zarniko, *Cent. f. Bacter. u. Parasitenk.*, 1889, Bd. VI, p. 227.

8 Escherich, *Cent. f. Bactericl. u. Parasitenk.*, 1890, Bd. VII, p. 11.

9 Klein, *Ibid.*, Bd. VII, Nos. 16 and 17, and *Nineteenth Annual Report of the Local Government Board for* 1889–90. Supplement containing the *Report of the Medical Officer for* 1889, p. 143.

species of bacilli, the one, found in all cases, doubtless identical with the Löffler bacillus, the other, found in 12 cases, probably, he thinks in his latest publication, identical with the pseudo-diphtheritic bacillus.

His description of both of these organisms can not be reconciled altogether with the statements of other observers. The bacillus found only in 12 cases, which he at first was inclined to identify with the Löffler bacillus, but which he now considers as the pseudo-diphtheritic bacillus, was found to be non-pathogenic for guinea-pigs, except in two instances, in which the autopsies showed entirely different appearances from those in animals inoculated with the diphtheritic bacillus. Klein's pseudo-diphtheritic bacillus does not grow at a temperature below 20° C.; it does not grow on potato; its colonies on gelatine and on agar resemble closely those of the genuine diphtheritic bacillus, which, however, is distinguishable by growing well at a temperature of 19°–20° C. and developing even at 16° C.; it produces in alkaline bouillon at 37° C. only slight cloudiness and forms flakes and granules, whereas his genuine diphtheritic bacillus grows more rapidly in bouillon, forming, after 24 hours, strong uniform turbidity; its cultures die out in a few months, whereas cultures of the true diphtheria bacillus survive at room-temperature for over 18 months; it presents fewer so-called degeneration and involution forms than the true bacillus. It will be observed that Klein's statement as to the growth of the two species in bouillon differs from that of Zarniko, and that he does not describe the characteristic growth of the true diphtheritic bacillus in bouillon. A culture of Klein's true bacillus of diphtheria examined by Löffler, was pronounced by him to be the genuine bacillus diphtheriæ.

Spronck[1] (1890) found in only one out of 13 cases of diphtheria, a non-virulent bacillus resembling the Löffler bacillus. Apparently solely on the ground of absence of virulence he designates this as the pseudo-diphtheritic bacillus. There were found in the same case and in all the other cases virulent diphtheritic bacilli.

Beck[2] (1890) says that he found the pseudo-diphtheritic bacillus in a large number of cases of diphtheria together with the virulent bacillus. In 66 healthy children the pseudo-diphtheritic bacillus was found 22 times and in 64 children with various non-diphtheritic affections of the mouth and throat it was found 14 times. In none of the latter 130 children was the virulent Löffler bacillus found once. The differential characters are essentially those given by Löffler, viz.: besides absence of viru ence, the pseudo-diphtheritic bacillus grows on blood-serum with more of a yellowish tint, on agar-agar much more rapidly and with colonies presenting more uniform, less notched margins than is the case with the genuine bacillus. Beck speaks of the color of these colonies as lighter ("heller") than that of the diphtheritic colonies. The rods are somewhat thicker than the Löffler bacilli but like these they vary in length.

Roux and Yersin[3] (1890) have made the most elaborate study of the relation between the virulent diphtheritic bacillus and the non-virulent forms.

Differences in the virulence of the Löffler bacillus as tested upon animals had been noted to some extent by previous investigators, especially by Brieger and Fraenkel.[4] Roux and Yersin examined 100 cases of diphtheria in all of which they found the Löffler bacillus. Cultures obtained from 40 out of 53 fatal cases were inoculated into guinea pigs, all of which succumbed in a period of time varying from less than 24 hours to four days. Cultures from 39 out of 47 cases which recovered, when tested upon guinea pigs, gave the following results: 17 of the cultures killed the animals in less than three days, seven in from four to nine days, five killed only some of the inoculated animals and ten produced only oedema varying from severe oedema followed by an eschar to a slight, quickly disappearing oedema, from which the animal recovered. They found the attenuated bacillus together with the virulent form less frequently in the fatal than in the mild cases and they noted in severe cases terminating in recovery a tendency for the attenuated bacilli to take the place of the virulent bacilli towards the end of the disease. They found the non-virulent, so-called pseudo-diphtheritic bacillus in the pharynx of 15 out of 45 children examined in the Hôpital des Enfants Malades in Paris and in 26 out of 59 children in a healthy village on the sea-coast where no diphtheria had occurred for a long time. The same bacillus was found once in ten of the attendants in the pavilion for diptheria, twice in six children affected with simple angina and five times in seven cases of measles. In all the non-diphtheritic cases the pseudo-diphtheritic bacilli were very scanty, rarely more than one to four colonies being present in a tube, and often only one colony in several tubes inoculated with mucus from the throat, so that they do not consider that the presence of the pseudo-diphtheritic bacillus causes any serious difficulty in the diagnosis of diphtheria by culture methods which show a large number of colonies of the specific bacillus in true diphtheria. Measles seem to offer an especially favorable soil for the development of the pseudo-diphtheritic bacillus. The only distinction which Roux and Yersin regard as of any weight between the so-called pseudo-diptheritic bacillus and the virulent diphtheritic bacillus, is the absence of virulence in the former. The colonies of both are identical on blood-serum, but the pseudo-diphtheritic bacillus is often shorter in colonies on this medium. The pseudo-diphtheritic bacillus grows usually, but not invariably more luxuriantly in bouillon, especially at the temperature of 20°–22° C., and produces a more voluminous deposit than is the case with the virulent bacillus. The changes in reaction of the bouillon from alkaline to acid, and then back to alkaline, occurs more quickly with the pseudo-diphtheritic form. In contradistinction from the aerobic growth, the development of the pseudo-diphtheritic bacillus in a vacuum is less abundant than that of the virulent species. The pseudo-diphtheritic bacillus does not produce toxic proteids in its cultures, and when inoculated subcutaneously into guinea-pigs, it is incapable of killing the animals, although it may cause sometimes more or less local œdema. As regards the question whether the so-called pseudo-diphtheritic bacillus and the virulent diphtheritic bacillus are two distinct species of bacteria, or whether the one is simply an attenuated form of the other, Roux and Yersin express themselves in favor of the latter view for the following reasons: the mere absence of virulence is not sufficient ground for separating one organism from another as a distinct species, and all alleged morphological and cultural differences between the pseudo-diphtheritic and the diphtheritic bacillus are too feeble and inconstant to distinguish them; all degrees of virulence exist between that capable of killing guinea-pigs in less than 24 hours to that causing only slight, temporary œdema at the point of inoculation; the gradual replacement of the virulent bacillus by one less virulent or completely attenuated as a case of diphtheria progresses toward recovery, speaks in favor of the doctrine of attenuation; the virulent diphtheritic bacillus can, although with much difficulty, be attenuated by a peculiar procedure outside of the body, so as to resemble the pseudo-diphtheritic bacillus, and finally diphtheritic bacilli so attenuated as to produce only local œdema without killing the animal may, by a combined inoculation with the erysipelas strepto-coccus, be made to acquire increased virulence so as to destroy guinea-pigs by inoculation. This transformation, however, has not been accomplished with the pseudo-diphtheritic bacillus devoid of all virulence, and until this has been done Roux and Yersin do not consider that the view which they advocate is fully proven.

It is apparent from the foregoing review of the literature of our subject that further investigations are needed to determine the nature of the so-called pseudo-diphtheritic bacillus or bacilli, and that the statements of various writers are conflicting. It is established that bacilli, with all the characters of the virulent Löffler bacillus, are to be found only very exceptionally in conditions where diphtheria is absent. In diphtheria several observers have found, together with genuine diphtheritic bacilli, bacilli resembling the Löffler bacillus, but devoid of virulence. Many have failed to find in the series of cases examined by them these non-virulent bacilli, others have found them very rarely, while von Hoffmann, and Roux and Yersin have obtained them not so very infrequently. Most of the German investigators have followed Löffler in considering these non-virulent bacilli found in diphtheria as a species distinct from the virulent diphtheritic bacilli, the distinction being based primarily upon the absence of virulence, but also upon slight morphological and cultural differences, the chief of which being more luxuriant and whiter growth upon agar-agar and capability of growth at lower temperatures. To these distinctions Zarniko adds the different modes of growth of the two organisms in bouillon. In general, the descriptions given of the non-virulent bacilli are unsatisfactory, and many observers seem to have gone little further than to determine the absence of virulence, and solely on this ground have designated the bacilli in question as pseudo-diphtheritic. As already mentioned, Klein's pseudo-diphtheritic bacillus can not, from his description, be identified with the

1 Spronck, *Centralbl. f. allg. Path. u. Patholog. Anat.*, 1890, Bd. I, p. 218.
2 Beck, *Zeit. f. Hyg.*, Bd. VIII, p. 434.
3 Roux and Yersin, *Annales de l'Institut Pasteur*, 1890, Tome IV, p. 409.
4 Brieger and Fraenkel, *Berliner Klin. Wochenschrift*, 1890, No. 11.

pseudo-diphtheritic bacillus of Löffler and of von Hoffmann. Roux and Yersin consider that the morphological and cultural differences between the diphtheritic and the pseudo-diphtheritic bacillus are inconstant and when present insufficient to establish different species. They expressly state that they have found in diphtheria bacilli absolutely indistinguishable from the Löffler bacilli, except by the absence of pathogenic properties when tested on animals.

It must be admitted that the morphological and cultural differences found by Löffler, von Hoffmann, and Zarniko to exist between the diphtheritic and the pseudo-diphtheritic bacilli lose much of their value by the variability in the properties of the virulent Löffler bacillus. This bacillus varies in size, in the readiness with which it grows at ordinary temperatures on gelatine and on agar-agar, in the luxuriance of its growth on these media and in the mode of its growth in bouillon which may be rendered diffusely cloudy instead of remaining clear with clumps at the sides and bottom of the tube.

Whereas the majority of investigators have found the pseudo-diphtheritic bacillus only rarely, von Hoffmann, Beck and Roux and Yersin, who have examined the largest number of cases, have found it not infrequently in healthy individuals, or in those with non-diphtheritic affections, so that it would seem to be, at least in some places a common inhabitant of the mouth and throat, although hardly a "regelmässiger Bewohner" of the pharynx as claimed by von Hoffmann. No differences have been determined between the pseudo diphtheritic bacillus found in some cases of diphtheria and that observed in other conditions, but upon this as upon many other points concerning the pseudo-diphtheritic bacillus, statements are often meagre or indefinite. It seems that the term pseudo-diphtheritic bacillus is now used loosely to designate a group of bacilli which resemble the Löffler bacillus, but which are without pathogenic properties when tested on guinea-pigs. The resemblance in morphology and cultural properties to the Löffler bacillus may amount to apparent identity, or there may be marked differences. It can hardly be otherwise than that such a loose usage must cover a variety of organisms, and that, therefore, the term itself must lack definite application.

Since the publication of the work upon the etiology of diphtheria by Prof. Welch and myself, I have devoted my time to the study of a number of cases of ordinary benign affections of the throat. These cases presented very slight constitutional symptoms, in fact, with two exceptions, were from the patients who daily visit the dispensary of the Johns Hopkins Hospital.

These studies were made, in all, upon 53 patients, 9 of whom were suffering from acute pharyngitis, 14 from acute follicular tonsillitis, 8 from ordinary post-nasal catarrh, 2 from simple enlarged tonsils, 15 from chronic pharyngitis, 1 from subacute laryngitis, 1 from chronic laryngitis, 1 from rhinitis, and 2 from an affection of the tonsils and pharynx which rendered a diagnosis without bacteriological aid more or less difficult.[1] The last two cases were described by the writer in a paper before the Johns Hopkins Hospital Medical Society, May 18th, 1891. They are inserted here for the purpose of completing the group.

For the examination of these 53 cases of various affections of the throat, the blood-serum mixture of Löffler was employed. The inoculations were conducted in the way common to this work.

In 49 of the cases of this group nothing of particular interest was observed. The tubes showed a variety of organisms, some of which are well known, particularly the pyogenic cocci, while others could not readily be identified. As they bore no immediate relations to the work under consideration they were dispensed with as soon as it was established that they were in no way to be confounded with the organism of diphtheria.

In four of these cases now to be described were found organisms which in their morphology and cultural peculiarities were so like the genuine bacillus diphtheriæ of Löffler that they were subjected to detailed study. The clinical histories of the cases and description of the organisms found in them are as follows:—

Case I.—J. B., aged 59 years, was admitted to the Johns Hopkins Hospital, March 19th, 1891, suffering from shortness of breath and moderate dropsy of the legs. Examination revealed hypertrophy of the heart with high-tension pulse, albuminuria and slight oedema of the lungs. At the end of two weeks he had improved considerably, but complained of slight fever and sore throat. His voice was husky and thick and he had some difficulty and pain in swallowing food. The pillars of the fauces, the uvula and tonsils were swollen and oedematous, of an intense crimson-red color and covered with a thin, grayish-white, slightly adherent material. There was a moderate elevation of temperature, not exceeding 102° F.

He was immediately isolated.

The soreness of the throat was of short duration, and in five days every vestige of the thin membranous-looking deposit had disappeared, no extension whatever having occurred during this time. He was discharged from the Hospital on April 18th, 1891.

Case II.—P. K. was well up to Sunday, April 19th. At 3 p. m., April 19th, he began to feel badly. There was a slight chill, no shaking, fever, slept badly. He complained of sore throat and pain upon swallowing. He had considerable headache and pain through the limbs and back. There was no bleeding from the nose, no cough, no vomiting. Bowels rather constipated. His temperature on admission to the ward was 104.8° F., pulse 112, full and bounding. Respiration quick, skin hot and moist, tongue clean and dry, face flushed.

Uvula, tonsils and pillars of the fauces injected and red and covered with a yellow, pultaceous deposit.

April 21st (the day following admission), temperature 100° F., pulse 100. Patient feels much better. He has had aconite and citrate of potash every 3 hours.

April 27th. Throat still sore—a grayish-white deposit over tonsils and pillars of fauces and soft palate.

April 29th. Patient discharged well.

Microscopic examination of cover-slip preparations from the deposit in the throat of each of these patients revealed the presence of a variety of organisms, among which could be made out the irregular curved, clubbed and spindle-forms common to the bacillus of Löffler. It may be said here that it is not safe to rely upon the microscopic examination alone of the smear preparations from these deposits, as there exist in the mouth, and particularly in the mouths of those having decayed teeth, curved and spindle-shaped bodies, the morphology of which is so like that of some of the forms common to the bacillus of Löffler that they might easily be mistaken for this organism.

In Case I cultures were made from the thin membranous deposit, the blood-serum mixture of Löffler being employed for the purpose. After 24 hours at 37° C., the tubes presented the appearance common to those made from an undoubted case, except, perhaps, there was an unusual number of colonies of the staphylococcus pyogenes aureus. From these blood-serum tubes there was but little difficulty in obtaining in pure culture an organism which in all of its morphological and cultural peculiarities was identical with the bacillus of Löffler, with a virulent culture of which it was constantly compared.

The colonies of this organism on nutrient glycerine agar-agar could not be distinguished from those resulting from the growth of the true organism of diphtheria.

In bouillon it presented the characteristic sedimentation and clumping without producing a diffuse clouding of the upper layers of the fluid.

On gelatine it did not produce liquefaction and its colonies were of the characteristic form.

It is non-motile.

On potato it grew in the way common to the bacillus of Löffler, as has been pointed out in the paper by Professor Welch and myself, as an invisible layer quite similar to that described for the bacillus of typhoid fever.

In short, it was not possible to differentiate by any of the culture methods at our disposal, between this organism and that described by Löffler.

The results, however, were different when this organism was inoculated into the subcutaneous tissues of guinea-pigs and kittens, both of which possess a marked susceptibility to the action of the b. diphtheriæ of Löffler.

Repeated inoculations of cultures of this organism growing on different media were negative, whereas the control animals inoculated with the cultures of the true diphtheria bacillus were positive in every case, the tissue changes being in each instance identical with those commonly following such inoculations.

From Case II the cover slips likewise presented a variety of organisms, and as in Case I a number of these were of a more or less suspicious appearance.

[1] I am indebted to Doctor Wm. Sidney Thayer, Resident Physician at the Johns Hopkins Hospital, for his valuable assistance in obtaining these cases for me.

The cultures from this case were upon glycerine agar-agar as there was at the time no blood-serum in the laboratory. After 24 hours at 37° C., the Esmarch tubes presented a striking appearance—they contained a moderate number of colonies of different appearance, the most conspicuous being those of a bright yellow color which proved to be made up of a coccus and a few others which presented an appearance which one might conceive to be that of the bacillus of diphtheria very much magnified. They were larger, denser, and much more moist and opaque than are those of the b. diphtheriæ.

Microscopic examination, however, of cover-slip preparations from those colonies showed them to be made up of an organism, the morphology of which is strikingly like that of the organism of diphtheria. All of the different curbed, pointed and spindle shapes were present as well as the large bizarre and broken involution forms so common to the true bacillus of diphtheria.

On the whole, however, these organisms are slightly larger than those of Löffler.

The growth of this organism on gelatine, agar-agar and blood-serum is so like that of the bacillus of Löffler that, excepting a greater degree of luxuriance, it is hardly possible at all times to tell the one from the other.

In bouillon there is macroscopically a tendency toward a diffuse clouding of the medium, but if a drop of this culture be examined microscopically without drying (as a hanging drop) it will be seen that the tendency throughout is to grow in minute clumps.

This organism is non-motile.

The most striking difference between this organism and the usual Löffler bacillus is its behavior toward potato.

On potato it grows with moderate rapidity as a dry, dirty-brown layer which eventually covers nearly the whole surface of the potato. It is finely granular on the surface and irregularly lobulated around its borders.

This is an appearance that we have failed to find with the ordinary bacillus of Löffler and likewise is it absent from the organism which has been described for Case I.

Like the organism from Case I when inoculated into guinea-pigs it has given us negative results, whereas the control animals inoculated at the same time with the true bacillus of diphtheria died with the characteristic lesions.

Case III.—F. B., girl, aet. 11 years, came into the outpatient department of this Hospital on June 2d, complaining of sore throat. Was taken sick June 1st.

Examination reveals reddening, injection and swelling of the tonsils. Small white plug in one of the crypts of left tonsil. Cervical lymphatics enlarged and painful. Temperature 99° F.

No evidence of a membrane anywhere to be found.

Diagnosis. Acute follicular tonsillitis.

June 5th. Child is reported well.

June 6th. Child is again seen. Examination reveals no trace of the acute process except a very minute white point over a crypt in left tonsil. Says she feels entirely well.

Cultures on Löffler's blood-serum mixture, from the plug on the left tonsil, from right tonsil and from the pharynx, shows after 48 hours at 38° C. (they were not examined after 24 hours) a number of large, dense, white, irregular and regular patches of growth which, upon microscopic examination, are seen to be made up of an organism, the morphology of which is strikingly suggestive of that of the bacillus of Löffler.

Other colonies composed of the small spindle-shape bacillus, so frequently seen in many of the cases of true diphtheria studied by Prof. Welch and myself were also present. Here and there colonies of streptococci were to be found. The macroscopic appearance of these tubes was similar to that of serum tubes from a case of true diphtheria, except, perhaps, the colonies having the appearance of those growing from the bacillus of Löffler were somewhat fewer in number.

Microscopic examination of these large, creamy colonies showed them to be made up of bacilli the morphological peculiarities of which were identical with those of the Löffler bacillus. The spindle and clubbed forms, likewise the irregularly segmented rods, were everywhere present. Very conspicuous were the dark, almost black, points seen in the individual bacilli when stained with Löffler's methylene-blue solution.

From these colonies three sets of agar-agar Esmarch tubes were made. After about 19 hours at 37° C. there appeared upon the tubes colonies in every way identical with those of the true diphtheria bacillus when seen under similar circumstances. Microscopically, these colonies were seen to be made up of organisms which could not be distinguished morphologically from the organism of Löffler. Under low magnifying power these colonies, when upon the surface of the agar, were irregularly round or oval with more or less notched periphery. They were granular and possessed a dark, granular, ragged centre, surrounded by a lighter peripheral zone. They were very flat and were elevated but slightly above the surface of the medium. They are not glazed, but rather dull in their appearance when seen by reflected light. When deep down in the agar they are round or oval, coarsely granular and of a more or less bronze color. This growth is not so rapid as that of the organisms from Case II.

On potato its growth is best described as producing a slight diminution in the reflective properties of the surface of the potato. Of eight potatoes inoculated with this organism six showed an invisible growth, whereas on the remaining two there was a very fine granular deposit not easily to be seen with the naked eye. In short, the cultural peculiarities of the organism found in this case were identical with those of the organism found in true diphtheria.

It is not pathogenic for guinea-pigs or kittens.

Case IV.—S. McS., male, adult. Clinical diagnosis of syphilitic pharyngitis. When he came to the dispensary the pharynx and both tonsils were injected. The tonsils slightly enlarged. No deposit anywhere in the throat.

Cultures from pharynx and tonsils gave a large number of colonies consisting of organisms which morphologically and in cultures are not distinguishable from the genuine diphtheritic bacillus. It sometimes clouds the bouillon and sometimes grows in the typical way in small macroscopic clumps. On blood-serum, agar-agar and gelatine it is not to be distinguished from the genuine diphtheria bacillus; it does not grow more luxuriantly, if anything less so than the Löffler bacillus. It grows invisibly on potato.

Two animals, guinea-pigs, were inoculated subcutaneously, each with one oese of a fresh culture on glycerine agar. The one culture was 24 hours, the other 48 hours old. These inoculations were made on June 27th and on July 13th. Neither animal presented any manifest effects from the inoculation, both having been kept under observation until August 7th, so that it is fair to assume that the organism is devoid of pathogenic properties.

From what we have seen in Cases I, III and IV, it is clear that there exists an organism indistinguishable from the genuine diphtheritic bacillus of Löffler, save by the absence of pathogenic properties.

The organism from Case II was easily distinguished from the bacillus of Löffler by its growth on potato, though in its morphology it was in many cases difficult to find any difference between the two.

From these observations we feel justified in agreeing with the opinion that has been advanced by other observers, particularly Hoffmann and Roux and Yersin, that under varying conditions the virulence of the true diphtheria bacillus may be observed to fluctuate in the degree of its intensity—at one time possessing the property in a high degree, at another presenting a decided attenuation and not unfrequently a complete absence of pathogenic power.

The organism obtained from Cases I, III and IV, we believe to be the true diphtheria bacillus which, from some unknown cause, has lost its virulence.

The organism obtained from Case II, though resembling closely the organism described by Löffler, presents a marked difference in its growth upon potato.

In the relation of these organisms to the ordinary staining reagents I can find no difference between them and the Löffler organism. They all stain readily by the Gram method and with the other dyes commonly employed in coloring bacteria. Their appearance when stained with Löffler's alkaline methylene-blue solution is identical. If one prepares cover-slip preparations from cultures of the same age on the same medium, the one from a true diphtheria culture, the other from the organisms just described, the only difference that one can detect is that the bacillus from Case II, which grows visibly on potato and on all other media, presents a slightly courser growth than is seen with the true diphtheria bacillus, is a little larger and presents occasionally more of the involution forms than does the Löffler organism.

The single point of distinction that can be made out between the organism obtained from Cases I, III, and IV and the true bacillus of diphtheria

is in the absence of pathogenic properties from the former, whereas in addition to this point of distinction the organism from Case II gives, as has been stated, a decided and distinct growth upon the surface of sterilized potato, an appearance which one does not see with the Löffler organism and which has thus far been absent from the organism obtained from the other cases.

In a paper recently read before the Johns Hopkins Hospital Medical Society [1] I expressed the opinion that while the organism obtained from the faucial deposit in Case II had under all circumstances grown as a visible deposit on potato and the genuine bacillus diphtheriæ of Löffler had in the great majority of cases given no naked-eye evidence of its growth on the same medium, still, as in the case of the typhoid bacillus, this apparent point of distinction may after subsequent work prove to be of more or less inconstancy and hence not so valuable a criterion for the differentiation of these organisms found in the faucial deposits as was at first supposed.

I have made a series of experiments with the view of shedding some light upon this subject:

From the single colonies on the Esmarch tubes made from the fauces of Case II six potatoes were inoculated. All grew *visibly* as a dirty brown, granular deposit. All were composed of organisms of the characteristic morphology of the genuine b. diphtheriæ. From one of these potatoes a set of Esmarch tubes on nutrient agar-agar was made. Upon these tubes there appeared two kinds of colonies, but *both made up of morphologically similar organisms.* One set of these colonies were fine, blue-white, transparent, flat, dry, concentrically arranged and somewhat irregular around their borders—in short, they were in every way identical with those colonies growing from the true b. diph. The other colonies on this tube were cream-white, moist, somewhat elevated above the surface, tolerably regular in outline and, by transmitted light, indistinctly concentric in their arrangement.

From the *finest and most characteristic* colonies on the Esmarch tubes a set of Esmarch tubes was made, likewise a set from the *coarser, cream-like colonies.* After 24 hours at 37° C. the appearance of the colonies on these two sets of Esmarch tubes were not only exactly alike, but they were in both cases identical with those growing from the ordinary virulent b. diph. of Löffler. After 72 to 96 hours, however, they had grown in both cases to an extent not commonly seen with the true b. diphtheriæ.

After 48 hours' growth the colonies on both sets of Esmarch tubes showed differences. In the same tube, for example, from the same source, some of the colonies retained their fine, delicate, characteristic structure, while others showed a tendency to grow more luxuriantly, so that the details of the colonies became lost. Throughout the growth of all of these colonies they presented to the platinum needle a peculiar dry or mealy feel.

An effort was now made to determine if possible the significance of these differences in the growth of the colonies on these tubes. The first test to which they were subjected was the behavior toward potatoes.

From the Esmarch tubes made from the coarse creamy colonies on the Esmarch tubes from the original potato which showed the brown growth, the *coarsest* colony was selected and from it four potatoes were inoculated. After 24 hours at 37° C., all four potatoes showed a visible growth similar to that on the original potato. After 72 hours at 37° C., this growth has increased to such an extent that it resembles closely the growth of the bact. coli commune on potato under the same conditions. Microscopically these growhs are composed of organisms of identically the morphology of the b. diphtheriæ.

The *finest* colony on this set of Esmarch tubes was at the same time selected and from it four potatoes were inoculated. After 24 hours at 37° C., no growth was visible. After 72 hours, however, at the same temperature, all four of them showed distinct characteristic development of the same organism.

From the other series of Esmarch tubes made from the *fine* characteristic colonies on the Esmarch tubes from the original potato which showed the brown growth the *coarsest* colony was selected and from it four potatoes were inoculated. After 24 hours, one grew distinctly visible, one grew doubtfully and two invisibly. After 72 hours at 37° C., all four showed visible growth.

From the same tubes the *finest* colony was selected and from it four potatoes were inoculated. After 24 hours, three grew invisibly and one grew just visibly. After 72 hours all showed distinct visible growth but on some of the potatoes it was more extensive than on others.

In this series of experiments the potatoes were from the same source and were all prepared in the same way and at the same time. They were all inoculated at the same time.

From a *virulent* culture of the b. diphtheriæ nine potatoes were inoculated. After 96 hours at 37° C., eight of these potatoes showed no visible growth, whereas one showed a growth which could just be made out upon its surface.

Reviewing the above experiments we find that in the majority of instances, if not quite constantly, the virulent organism is seen to grow invisibly on potato—now and then a very indistinct growth may be made out. Twice in a large number of inoculations upon potatoes have I seen it grow visibly, but even then its growth could only be seen with great difficulty. Among the descendants from the potato, from the original Esmarch tubes, from the patient (Case II), every grade of development upon potatoes under the same conditions are seen—from the very fine, almost invisible growth, up to the coarse growth, resembling that of the bact. coli commune.

Microscopically, no difference can be made out between the organisms comprising these potato cultures.

Whether these differences in the development of these organisms upon potato can be taken as indicating different degrees of departure from the pathogenic condition as seen in the genuine bacillus of Löffler, it is impossible to say as no regular or corresponding deviation in the periods of incubation of these different organisms in the bodies of animals could be made out, because, as has been stated, they were all without pathogenic properties.

During the course of this work efforts were made to determine if the inoculation of susceptible animals, with the cultures of these organisms which are so like the bacillus of Löffler, would have any effect in the production of immunity in these animals toward the subsequent inoculation of virulent cultures of the genuine b. diphtheriæ.

Though the work can hardly be said to have been conducted on a very large scale, still the evidence obtained in these experiments does not confirm such an opinion.

Variations in the length of time which ensued between the time of inoculation and death of these animals, which were first treated with the non-virulent and subsequently with the virulent cultures, could be seen, but they were too slight in their degree to lead one to suppose that they were due to any protection afforded to the animal by the non-virulent cultures with which it had been inoculated.

[1] "The Relation of the Pseudo-Diphtheritic Bacillus to the Diphtheritic Bacillus," by A. C. Abbott, M. D., Assistant in Bacteriology and Hygiene, Johns Hopkins Hospital. *Johns Hopkins Hospital Bulletin*, No. 15, August, 1891.

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